Application No. 10/773,761 Reply dated July 20, 2010 Reply to Notice dated July 7, 2010

## **Amendments to the Claims:**

This listing of claims will replace all prior versions, and listings of claims in the application:

## **Listing of Claims:**

1-13. (Canceled)

14. (Currently amended) A method to determine outcome of a human subject having ER+ (estrogen receptor positive) breast cancer if treated with an antiestrogen-agent aromatase inhibitor against breast cancer, or of a human subject afflicted with breast cancer and treated with an antiestrogen agent against breast cancer, said method comprising:

producing cDNA copies of <u>HoxB13 and IL17BR</u> <u>mRNA</u> from a sample of <u>ER+ (estrogen receptor positive)</u> breast cancer cells from said human subject,

determining a ratio of HoxB13 to IL17BR mRNA expression levels based on said cDNA copies, and

wherein a ratio of HoxB13 and IL17BR-RNA-expression levels, based on said eDNA eopies, that is below the

determining the ratio as higher than a mean (average) ratio of HoxB13 and IL17BR RNA expression levels in ER+ breast cancer cells and as indicating indicates a cancer free outcome, and

a ratio above the mean (average) ratio of HoxB13 and IL17BR-RNA expression levels, based on said eDNA copies, in ER+ breast cancer cells indicates an outcome comprising cancer recurrence that is non-responsive to said aromatase inhibitor;

wherein said mean (average) ratio of HoxB13 and IL17BR RNA expression levels is determined from [[the]] a mean (average) of HoxB13 mRNA expression levels, and [[the]] a mean (average) of IL17BR mRNA expression levels, in ER+ breast cancer cell samples from human breast cancer subjects that responded to treatment with said antiestrogen agent aromatase inhibitor against breast cancer and from human breast cancer subjects that [[do]] did not respond to treatment with said antiestrogen agent aromatase inhibitor.

15. (Canceled).

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- 16. (Currently amended) The method of claim 14 wherein said antiestrogen agent against breast cancer is selected from a selective estrogen receptor modulator (SERM), selective estrogen receptor downregulator (SERD), or aromatase inhibitor (AI) is a non-steroidal agent.
  - 17. (Canceled).
- 18. (Previously presented) The method of claim 14 wherein said cDNA copies of HoxB13 and IL17BR RNA are used for RNA amplification from said sample of breast cancer cells.
- 19. (Previously presented) The method of claim 14 wherein said cDNA copies of HoxB13 and IL17BR RNA are used in quantitative PCR.
- 20. (Previously presented) The method of claim 19 wherein said quantitative PCR is real-time PCR and said ratio of HoxB13 and IL17BR RNA expression levels is expressed as a  $\Delta C_1$  of the  $C_1$  values for HoxB13 and IL17BR RNA expression levels.
- 21. (Previously presented) The method of claim 14 wherein said sample is a formalin fixed paraffin embedded (FFPE) sample.
- 22. (Original) The method of claim 14 wherein said sample is obtained by a minimally invasive technique or selected from core biopsy, excisional biopsy, a ductal lavage sample, a fine needle aspiration sample, or cells microdissected from said sample.
- 23. (Currently amended) A method to predict an expected response or lack of response to treatment with an antiestrogen agent aromatase inhibitor against breast cancer in a human ER+ (estrogen receptor positive) breast cancer patient, said method comprising

determining an expected non-response to treatment with an antiestrogen agent against breast cancer for said patient by producing cDNA copies of <u>HoxB13 and IL17BR</u> mRNA from a sample of <u>ER+ (estrogen receptor positive)</u> breast cancer cells from said patient, [[and]]

determining, based on said eDNA copies, a ratio of HoxB13 and IL17BR RNA expression levels based on said cDNA copies, and

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determining the ratio as that is higher than [[the]] a mean (average) ratio of HoxB13 and IL17BR RNA expression in ER+ breast cancer cells and as indicating said cancer as expected to lack response to treatment with said aromatase inhibitor; and/or

determining an expected response to treatment with said antiestrogen agent against breast cancer for said patient by producing cDNA copies of mRNA from a sample of breast cancer cells from said patient and determining, based on said cDNA copies, a ratio of HoxB13 and IL17BR-RNA expression levels that is lower than the mean (average) ratio of HoxB13 and IL17BR expression in ER+ breast cancer cells

wherein said mean (average) ratio of HoxB13 and IL17BR RNA expression levels is determined from [[the]] a mean (average) of HoxB13 mRNA expression levels, and [[the]] a mean (average) of IL17BR mRNA expression levels, in ER+ breast cancer cell samples from human breast cancer subjects that responded to treatment with said antiestrogen agent aromatase inhibitor against breast cancer and from human breast cancer subjects that [[do]] did not respond to treatment with said antiestrogen agent aromatase inhibitor.

- 24. (Canceled).
- 25. (Currently amended) The method of claim 24 wherein said antiestrogen agent against breast cancer is selected from a selective estrogen receptor-modulator (SERM), selective estrogen receptor downregulator (SERD), or aromatase inhibitor (AI) is a non-steroidal agent.
  - 26. (Canceled).
- 27. (Previously presented) The method of claim 24 wherein said cDNA copies of HoxB13 and IL17BR RNA are used for RNA amplification from said sample of breast cancer cells.
- 28. (Previously presented) The method of claim 24 wherein said cDNA copies of HoxB13 and IL17BR RNA are used in quantitative PCR.
- 29. (Previously presented) The method of claim 28 wherein said quantitative PCR is real-time PCR and said ratio of HoxB13 and IL17BR RNA expression levels is expressed as a  $\Delta C_t$  of the  $C_t$  values for HoxB13 and IL17BR RNA expression levels.

- 30. (Previously presented) The method of claim 24 wherein said sample is a formalin fixed paraffin embedded (FFPE) sample.
- 31. (Original) The method of claim 24 wherein said sample is obtained by a minimally invasive technique or selected from core biopsy, excisional biopsy, a ductal lavage sample, a fine needle aspiration sample, or cells microdissected from said sample.

32-51. (Canceled).

- 52. (Currently amended) The method of claim 14 wherein said assaying comprises detecting expression of cDNA copies comprise a HoxB13 sequence selected from SEQ ID NOS: 6, 7, 10, 11-31, 35 or 37.
- 53. (Currently amended) The method of claim 14 wherein said assaying comprises detecting expression of cDNA copies comprise an IL17BR sequence selected from SEQ ID NOs: 1, 2, 3, or 8, or 32-34.
- 54. (Currently amended) The method of claim 23 wherein said assaying emprises detecting expression of cDNA copies comprise a HoxB13 sequence selected from SEQ ID NOS: 6, 7, 10, 11-31, 35 or 37.
- 55. (Currently amended) The method of claim 23 wherein said assaying comprises detecting expression of cDNA copies comprise an IL17BR sequence selected from SEQ ID NOs: 1, 2, 3, or 8, or 32-34.

56-61. (Canceled).

62. (Currently amended) The method of claim 14 wherein said assaying is by determining a ratio of HoxB13 to IL17BR mRNA expression levels based on cDNA copies comprises hybridization of said cDNA copies to a polynucleotide comprising sequences of at least 15 nucleotides from the 3' untranslated region, the coding region, or the 5' untranslated region of human HoxB13 or IL17BR sequences.

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- 63. (Currently amended) The method of claim 23 wherein said assaying is by determining a ratio of HoxB13 and IL17BR RNA expression levels based on said cDNA copies comprises hybridization of said cDNA copies to a polynucleotide comprising sequences of at least 15 nucleotides from the 3' untranslated region, the coding region, or the 5' untranslated region of human HoxB13 or IL17BR sequences.
  - 64-68. (Canceled).
- 69. (Currently amended) The method of claim <u>25 wherein said non-steroidal agent</u> is selected from anastrozole, letrozole, and vorozole <del>29 wherein said antiestrogen agent is tamoxifen</del>.
  - 70. (Canceled).
  - 71. (New) The method of claim 69 wherein said non-steroidal agent is letrozole.
- 72. (New) The method of claim 16 wherein said non-steroidal agent is selected from anastrozole, letrozole, and vorozole.
  - 73. (New) The method of claim 72 wherein said non-steroidal agent is letrozole.